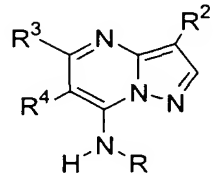
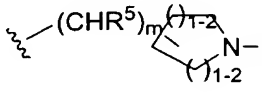
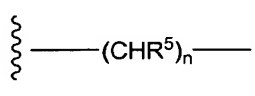
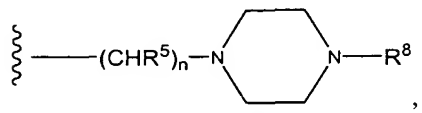
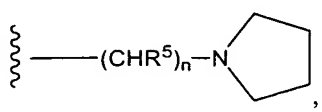
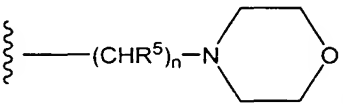
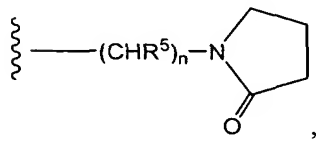
CLAIMS

What is claimed is:

1. A compound represented by the structural formula:

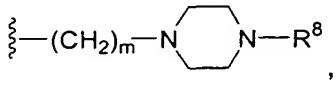


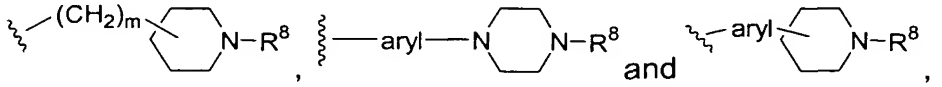
or a pharmaceutically acceptable salt or solvate of said compound, wherein:

R is H, alkyl, alkenyl, alkynyl, arylalkyl, arylalkenyl, cycloalkyl, cycloalkylalkyl, alkenylalkyl, alkynylalkyl, heterocyclyl, heterocyclylalkyl, heteroarylalkyl (including N-oxide of said heteroaryl), -$(CHR^5)_n$-aryl, -$(CHR^5)_n$-heteroaryl,  ,  ,  ,  ,  or  ,

wherein each of said alkyl, alkenyl, alkynyl, aryl, cycloalkyl, heterocyclyl, and heteroaryl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, heterocyclylalkyl, CF_3, OCF_3, CN, -OR^5, -NR^5R^{10}, -$C(R^4R^5)_p$-R^9, -$N(R^5)$Boc, -$(CR^4R^5)_pOR^5$, -$C(O_2)R^5$, -$C(O)R^5$, -$C(O)NR^5R^{10}$, -SO_3H, -SR^{10}, -$S(O_2)R^7$, -$S(O_2)NR^5R^{10}$, -$N(R^5)S(O_2)R^7$, -$N(R^5)C(O)R^7$ and -$N(R^5)C(O)NR^5R^{10}$;

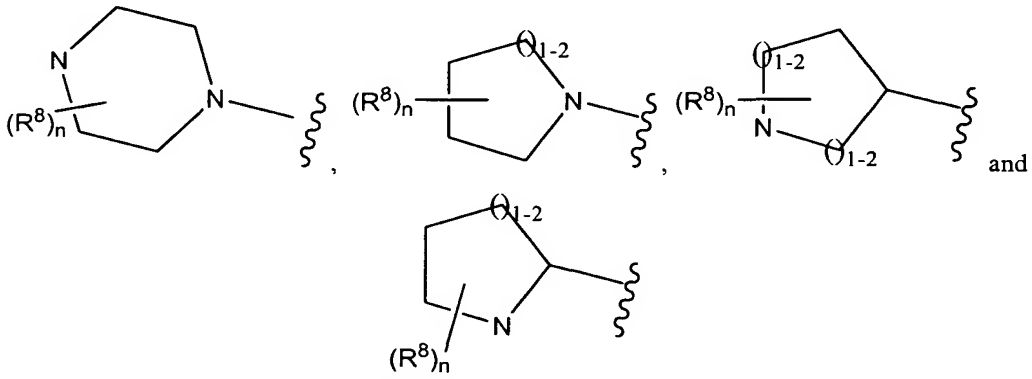
R^2 is selected from the group consisting of R^9, alkyl, alkenyl, alkynyl, CF_3, heterocyclyl, heterocyclylalkyl, halogen, haloalkyl, aryl, arylalkyl, heteroarylalkyl, alkynylalkyl, cycloalkyl, heteroaryl, alkyl substituted with 1-6 R^9 groups which can be the same or different and are independently selected from the list of R^9 shown below, aryl substituted with 1-3 aryl or heteroaryl groups which can be the

same or different and are independently selected from phenyl, pyridyl, thiophenyl, furanyl and thiazolo groups, aryl fused with an aryl or heteroaryl group, heteroaryl substituted with 1-3 aryl or heteroaryl groups which can be the same or different and are independently selected from phenyl, pyridyl, thiophenyl, furanyl and thiazolo groups, heteroaryl fused with an aryl or heteroaryl group,  ,

 ,

wherein one or more of the aryl and/or one or more of the heteroaryl in the above-noted definitions for R^2 can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, -CN, $-OR^5$, $-SR^5$, $-S(O_2)R^6$, $-S(O_2)NR^5R^6$, $-NR^5R^6$, $-C(O)NR^5R^6$, CF_3, alkyl, aryl and OCF_3;

R^3 is selected from the group consisting of H, halogen, $-NR^5R^6$, $-OR^6$, $-SR^6$, $-C(O)N(R^5R^6)$, alkyl, alkynyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl,



wherein each of said alkyl, cycloalkyl, aryl, arylalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl and heteroarylalkyl for R^3 and the heterocyclyl moieties whose structures are shown immediately above for R^3 can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF_3, CN, $-OCF_3$,

$-(CR^4R^5)_pOR^5$, $-OR^5$, $-NR^5R^6$, $-(CR^4R^5)_pNR^5R^6$, $-C(O_2)R^5$, $-C(O)R^5$, $-C(O)NR^5R^6$, $-SR^6$, $-S(O_2)R^6$, $-S(O_2)NR^5R^6$, $-N(R^5)S(O_2)R^7$, $-N(R^5)C(O)R^7$ and $-N(R^5)C(O)NR^5R^6$, with the proviso that no carbon adjacent to a nitrogen atom on a heterocyclyl ring carries a $-OR^5$ moiety;

R^4 is H, halo or alkyl;

R^5 is H, alkyl, aryl or cycloalkyl;

R^6 is selected from the group consisting of H, alkyl, alkenyl, aryl, arylalkyl, arylalkenyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl, wherein each of said alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, heterocyclylalkyl, CF_3, OCF_3, CN, $-OR^5$, $-NR^5R^{10}$, $-C(R^4R^5)_p-R^9$, $-N(R^5)$Boc, $-(CR^4R^5)_pOR^5$, $-C(O_2)R^5$, $-C(O)R^5$, $-C(O)NR^5R^{10}$, $-SO_3H$, $-SR^{10}$, $-S(O_2)R^7$, $-S(O_2)NR^5R^{10}$, $-N(R^5)S(O_2)R^7$, $-N(R^5)C(O)R^7$ and $-N(R^5)C(O)NR^5R^{10}$;

R^{10} is selected from the group consisting of H, alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl, wherein each of said alkyl, aryl, arylalkyl, cycloalkyl, heterocyclyl, heterocyclylalkyl, heteroaryl, and heteroarylalkyl can be unsubstituted or optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, heterocyclylalkyl, CF_3, OCF_3, CN, $-OR^5$, $-NR^4R^5$, $-C(R^4R^5)_p-R^9$, $-N(R^5)$Boc, $-(CR^4R^5)_pOR^5$, $-C(O_2)R^5$, $-C(O)NR^4R^5$, $-C(O)R^5$, $-SO_3H$, $-SR^5$, $-S(O_2)R^7$, $-S(O_2)NR^4R^5$, $-N(R^5)S(O_2)R^7$, $-N(R^5)C(O)R^7$ and $-N(R^5)C(O)NR^4R^5$;

or optionally (i) R^5 and R^{10} in the moiety $-NR^5R^{10}$, or (ii) R^5 and R^6 in the moiety $-NR^5R^6$, may be joined together to form a cycloalkyl or heterocyclyl moiety, with each of said cycloalkyl or heterocyclyl moiety being unsubstituted or optionally independently being substituted with one or more R^9 groups;

R^7 is selected from the group consisting of alkyl, cycloalkyl, aryl, arylalkenyl, heteroaryl, arylalkyl, heteroarylalkyl, heteroarylalkenyl, and

heterocyclyl, wherein each of said alkyl, cycloalkyl, heteroarylalkyl, aryl, heteroaryl and arylalkyl can be unsubstituted or optionally independently substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, alkyl, aryl, cycloalkyl, CF_3, OCF_3, CN, $-OR^5$, $-NR^5R^{10}$, $-CH_2OR^5$, $-C(O_2)R^5$, $-C(O)NR^5R^{10}$, $-C(O)R^5$, $-SR^{10}$, $-S(O_2)R^{10}$, $-S(O_2)NR^5R^{10}$, $-N(R^5)S(O_2)R^{10}$, $-N(R^5)C(O)R^{10}$ and $-N(R^5)C(O)NR^5R^{10}$;

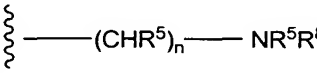
R^8 is selected from the group consisting of R^6, $-OR^6$, $-C(O)NR^5R^{10}$, $-S(O_2)NR^5R^{10}$, $-C(O)R^7$, $-C(=N\text{-}CN)\text{-}NH_2$, $-C(=NH)\text{-}NHR^5$, heterocyclyl, and $-S(O_2)R^7$;

R^9 is selected from the group consisting of halogen, -CN, $-NR^5R^{10}$, $-C(O_2)R^6$, $-C(O)NR^5R^{10}$, $-OR^6$, $-SR^6$, $-S(O_2)R^7$, $-S(O_2)NR^5R^{10}$, $-N(R^5)S(O_2)R^7$, $-N(R^5)C(O)R^7$and $-N(R^5)C(O)NR^5R^{10}$;

m is 0 to 4;

n is 1 to 4; and

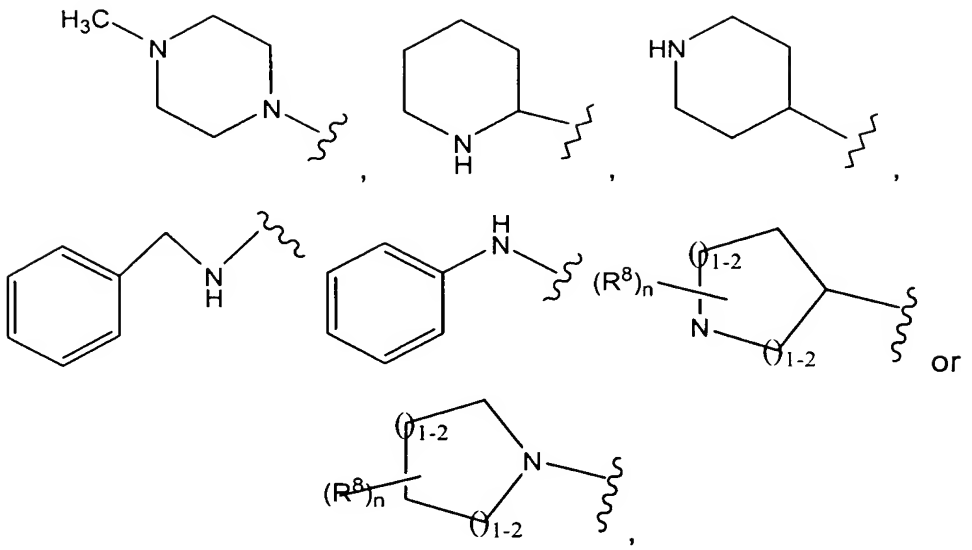
p is 1 to 4,

with the proviso that when R^2 is phenyl, R^3 is not alkyl, alkynyl or halogen, and that when R^2 is aryl, R is not  , and with the further proviso that when R is arylalkyl, then any heteroaryl substituent on the aryl of said arylalkyl contains at least three heteroatoms.

2. The compound of claim 1, wherein R is $-(CHR^5)_n$-aryl, $-(CHR^5)_n$-heteroaryl, alkyl, cycloalkyl, heterocyclyl, or heteroarylalkyl (including N-oxide of said heteroaryl), wherein each of said alkyl, aryl, cycloalkyl, heterocyclyl and heteroaryl can be unsubstituted or optionally substituted with one or more moieties as stated in claim 1;

R^2 is halogen, alkyl, haloalkyl, CN, cycloalkyl, heterocyclyl or alkynyl;

R^3 is H, lower alkyl, aryl, heteroaryl, cycloalkyl, $-NR^5R^6$,



wherein said alkyl, aryl, heteroaryl, cycloalkyl and the heterocyclyl structures shown immediately above for R^3 are optionally substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of halogen, CF_3, OCF_3, lower alkyl, CN, $-C(O)R^5$, $-S(O_2)R^5$, $-C(=NH)-NH_2$, $-C(=CN)-NH_2$, hydroxyalkyl, alkoxycarbonyl, $-SR^5$, and OR^5, with the proviso that no carbon adjacent to a nitrogen atom on a heterocyclyl ring carries a $-OR^5$ moiety;

R^4 is H or lower alkyl;

R^5 is H, lower alkyl or cycloalkyl;

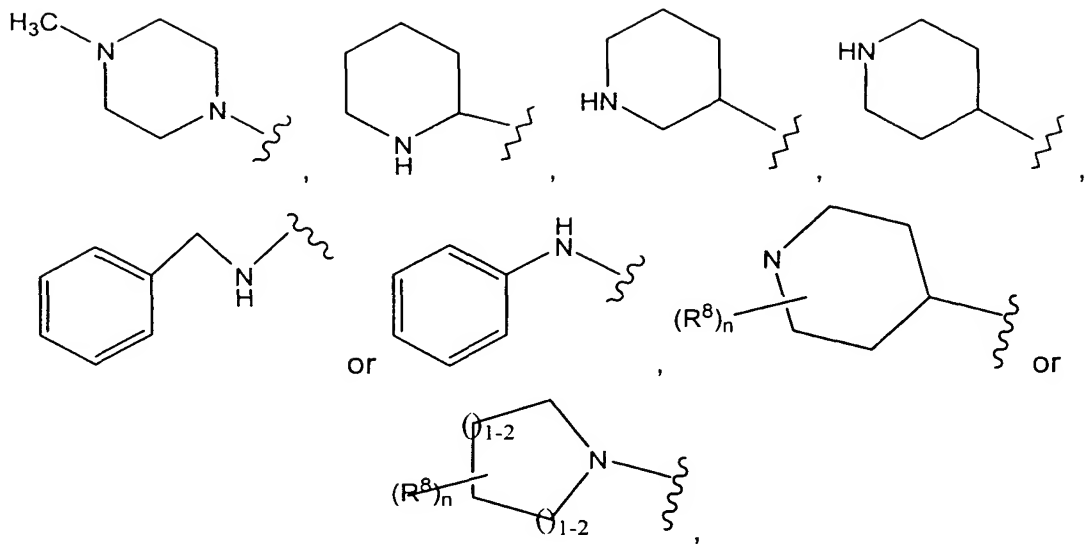
n is 1 to 2; and

p is 1 or 2.

3. The compound of claim 2, wherein R is hydroxyalkyl, $-(CHR^5)_n$-aryl, or $-(CHR^5)_n$-heteroaryl, wherein each of said aryl and heteroaryl is unsubstituted or substituted with one or more groups which can be the same or different, each group being independently selected from the group consisting of heteroaryl, amine, heterocyclyl, $-C(O)N(R^5R^6)$, $-S(O_2)R^5$, $-S(O_2)N(R^5R^6)$, alkoxy and halo.

4. The compound of claim 2, wherein R^2 is Br, Cl, CF_3, CN, lower alkyl, cyclopropyl, alkynyl, alkyl substituted with $-OR^6$ or tetrahydrofuranyl.

5. The compound of claim 2, wherein R^3 is H, lower alkyl, aryl, heteroaryl, cycloalkyl,



wherein each of said alkyl, aryl, heteroaryl, cycloalkyl and the heterocyclyl structures shown immediately above for R^3 are optionally substituted with one or more moieties which moieties can be the same or different, each moiety being independently selected from the group consisting of halogen, CF_3, OCF_3, lower alkyl, CN and OR^5, with the proviso that no carbon adjacent to a nitrogen atom on a heterocyclyl ring carries a – OR^5 moiety.

6. The compound of claim 2, wherein R^4 is H or lower alkyl.

7. The compound of claim 2, wherein R^5 is H.

8. The compound of claim 2, wherein n is 1.

9. The compound of claim 1, wherein p is 1.

10. The compound of claim 2, wherein R is benzyl or hydroxyalkyl.

11. The compound of claim 2, wherein R is pyrid-3-ylmethyl, wherein said pyridyl may be unsubstituted or optionally independently substituted with one or more moieties as stated in claim 1.

12. The compound of claim 2, wherein R is pyrid-4-ylmethyl, wherein said pyridyl may be unsubstituted or optionally independently substituted with one or more moieties as stated in claim 1.

13. The compound 2, wherein R is the N-oxide of pyrid-2-ylmethyl, pyrid-3-ylmethyl, or pyrid-4-ylmethyl, wherein each of said pyridyl may be unsubstituted or optionally independently substituted with one or more moieties as stated in claim 1.

14. The compound of claim 4, wherein said R^2 is Br.

15. The compound of claim 4, wherein said R^2 is Cl.

16. The compound of claim 4, wherein R^2 is ethyl.

17. The compound of claim 4, wherein R^2 is cyclopropyl.

18. The compound of claim 4, wherein R^2 is ethynyl.

19. The compound of claim 2, wherein R^3 is lower alkyl, cycloalkyl, heterocyclyl, aryl or $-N(R^5R^6)$.

20. The compound of claim 19, wherein R^3 is isopropyl.

21. The compound of claim 19, wherein R^3 is cyclohexyl or norbornyl wherein each of said cyclohexyl or norbornyl can be unsubstituted or substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of alkyl and hydroxyalkyl.

22. The compound of claim 19, wherein R^3 is unsubstituted phenyl.

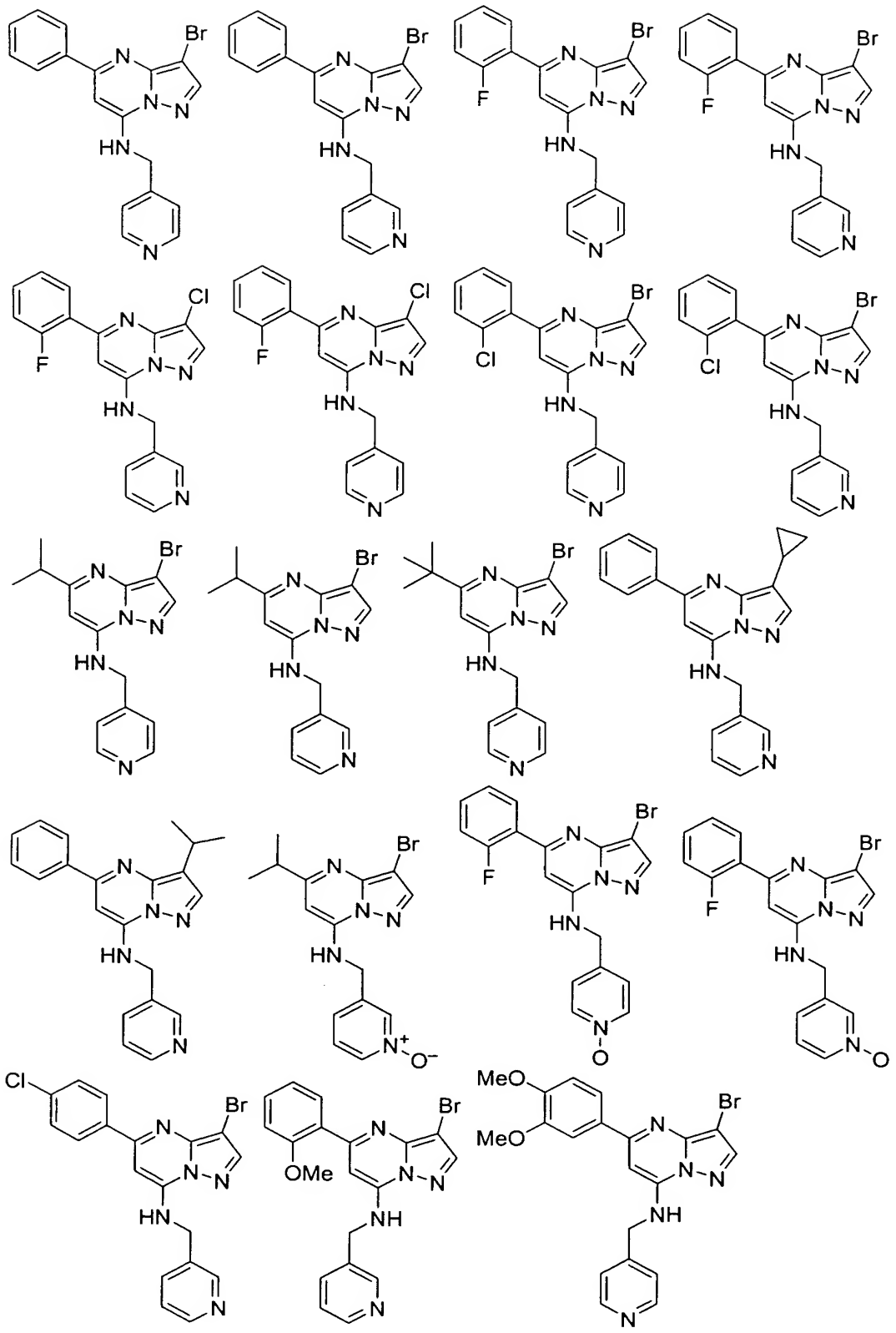
23. The compound of claim 19, wherein R^3 is a phenyl substituted with one or moieties which can be the same or different, each moiety being independently selected from the group consisting of F, Br, Cl and CF_3.

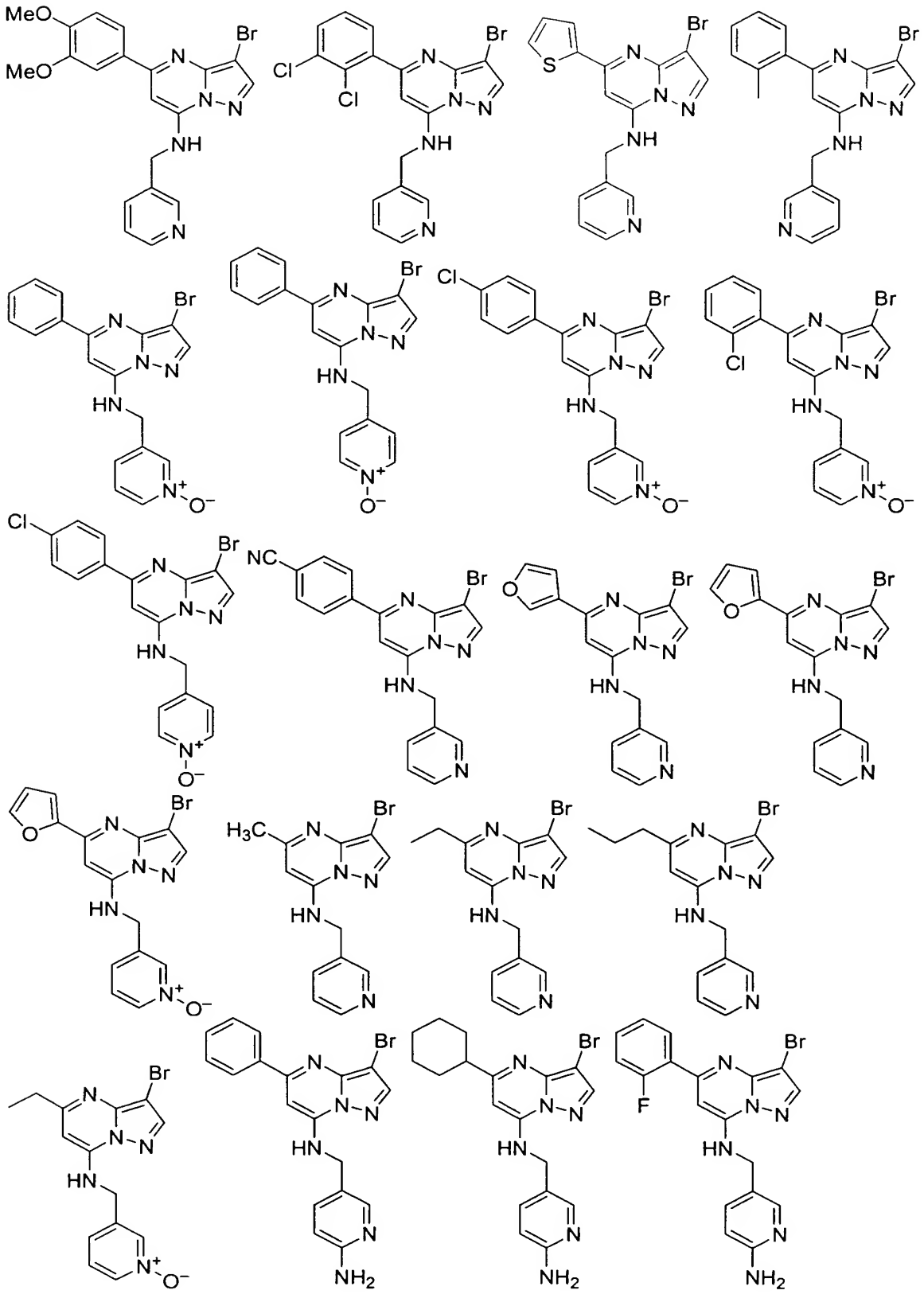
24. The compound of claim 19, wherein R^5 of said $-N(R^5R^6)$ is H or hydroxyalkyl, and R^6 of said $-N(R^5R^6)$ is selected from the group consisting of alkyl, hydroxyalkyl, cycloalkyl and methylenedioxy, wherein each of said alkyl and cycloalkyl can be unsubstituted or substituted with one or more moieties which can be the same or different, each moiety being independently selected from the group consisting of amine, ethoxycarbonyl, amide, hydroxyalkyl, hydroxy,

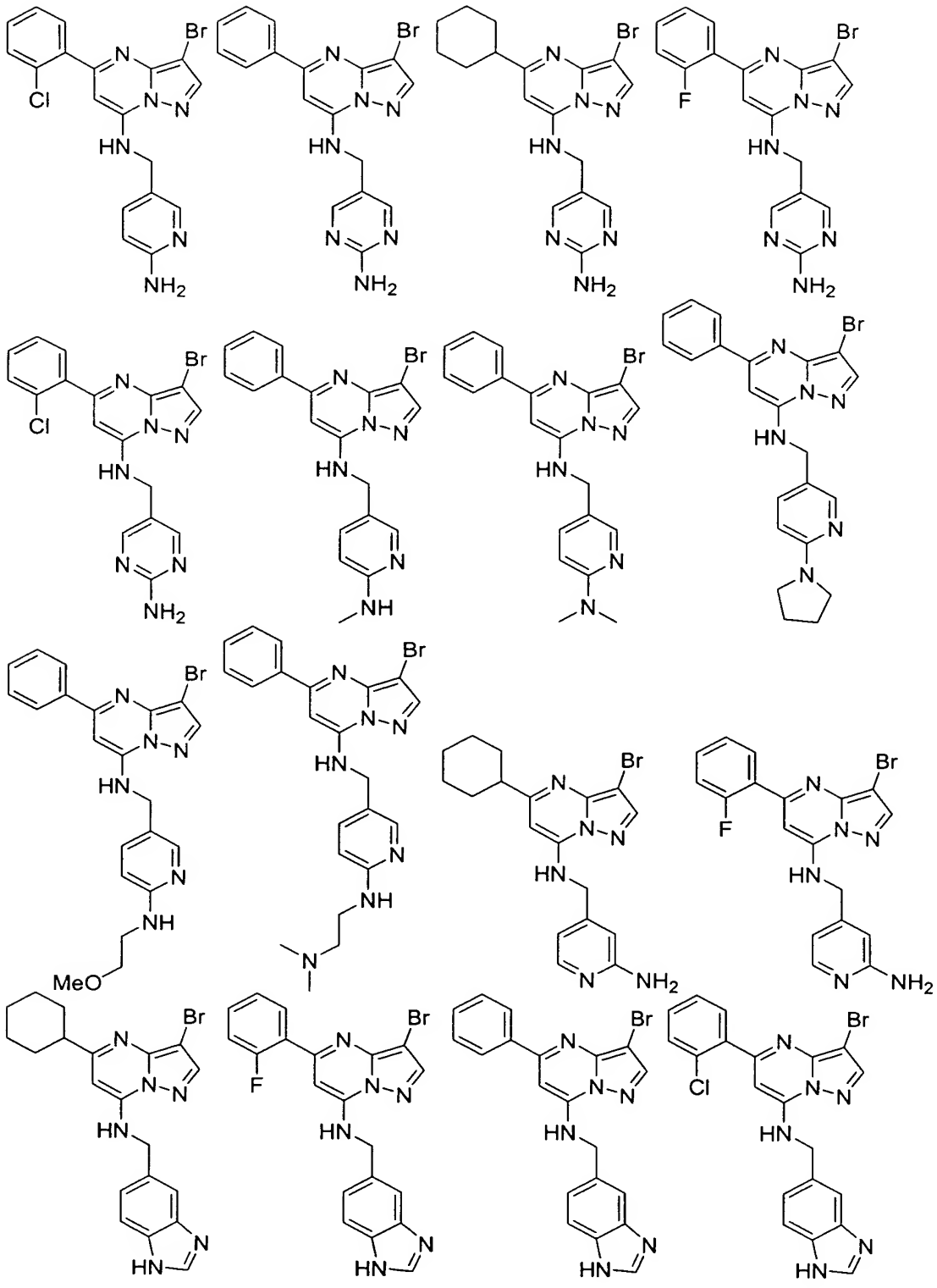
25. The compound of claim 19, wherein R^5 and R^6 of said $-N(R^5R^6)$ are joined together to form a heterocyclyl moiety, wherein said heterocyclyl moiety can be unsubstituted or optionally independently substituted with one or more groups which can be the same or different, each group being selected from the group consisting of hydroxyalkyl, amide, $-C(O)R^5$, $>C(CH_3)_2$, $-S(O_2)R^5$, $-S(O_2)N(R^5R^6)$, $-C(=NH)N(R^5R^6)$ and $-C(=N\text{-}CN)N(R^5R^6)$.

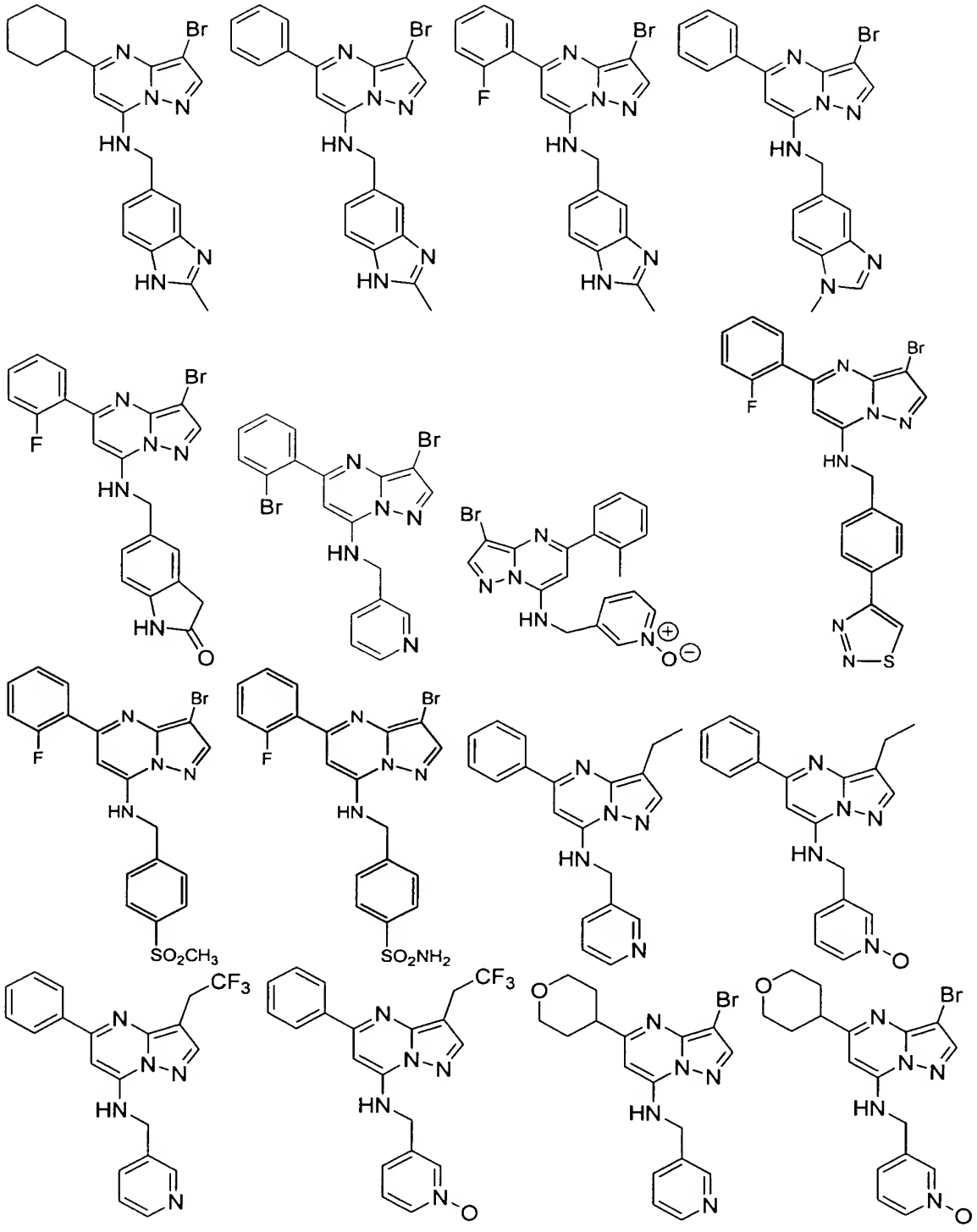
26. The compound of claim 25, wherein said heterocyclyl moiety formed by R^5 and R^6 is a pyrrolidine or piperidine ring.

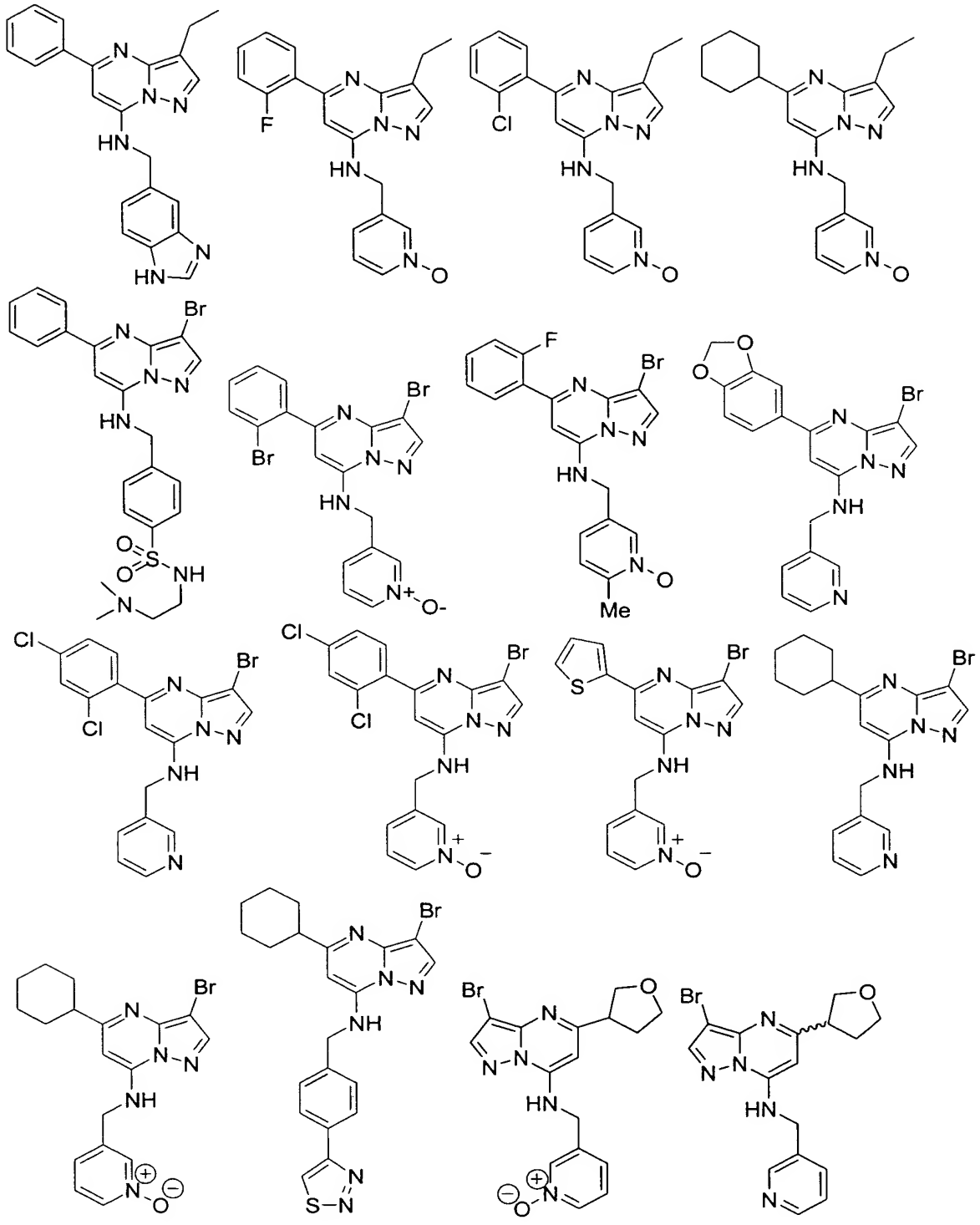
27. A compound of the formula:

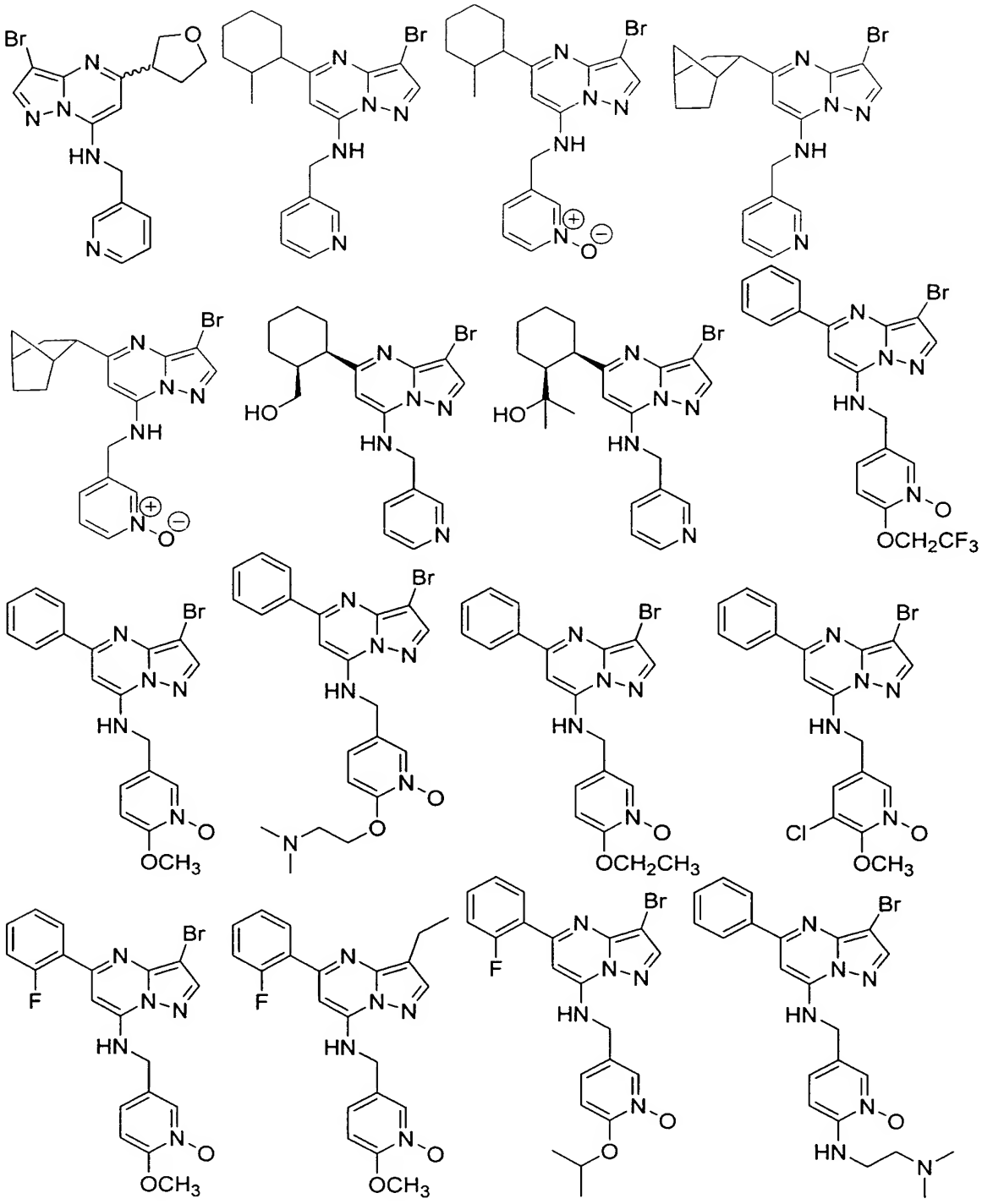


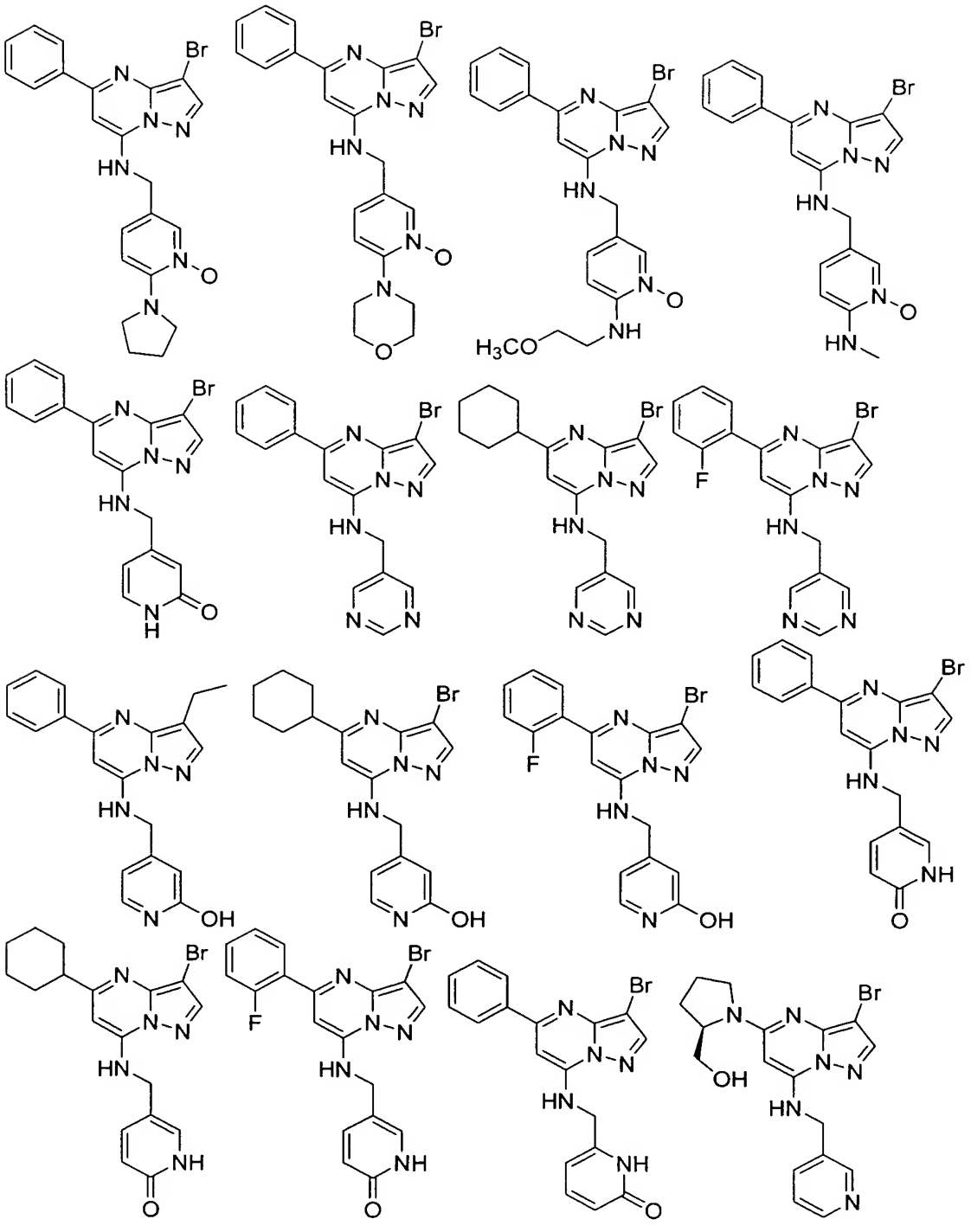


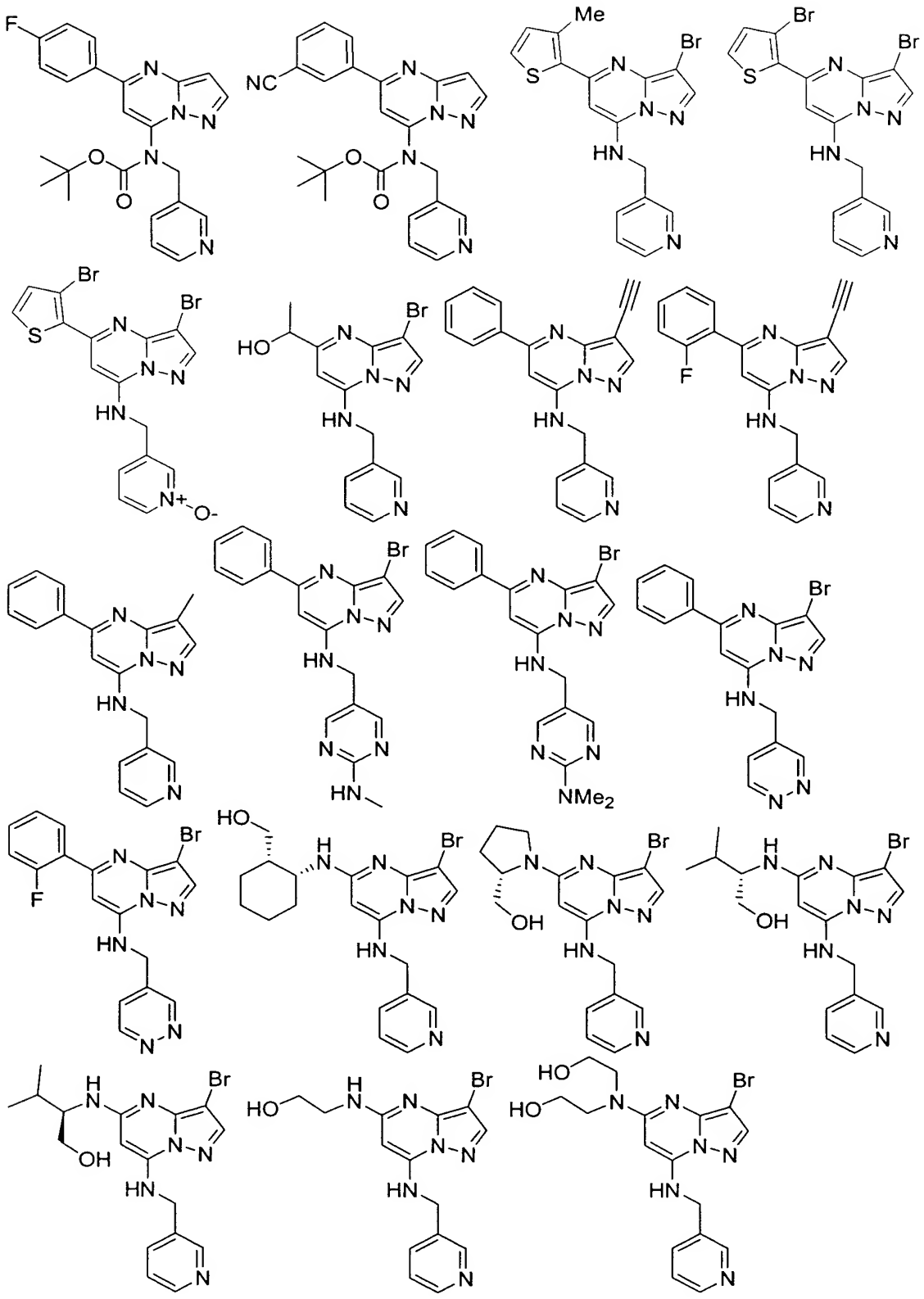


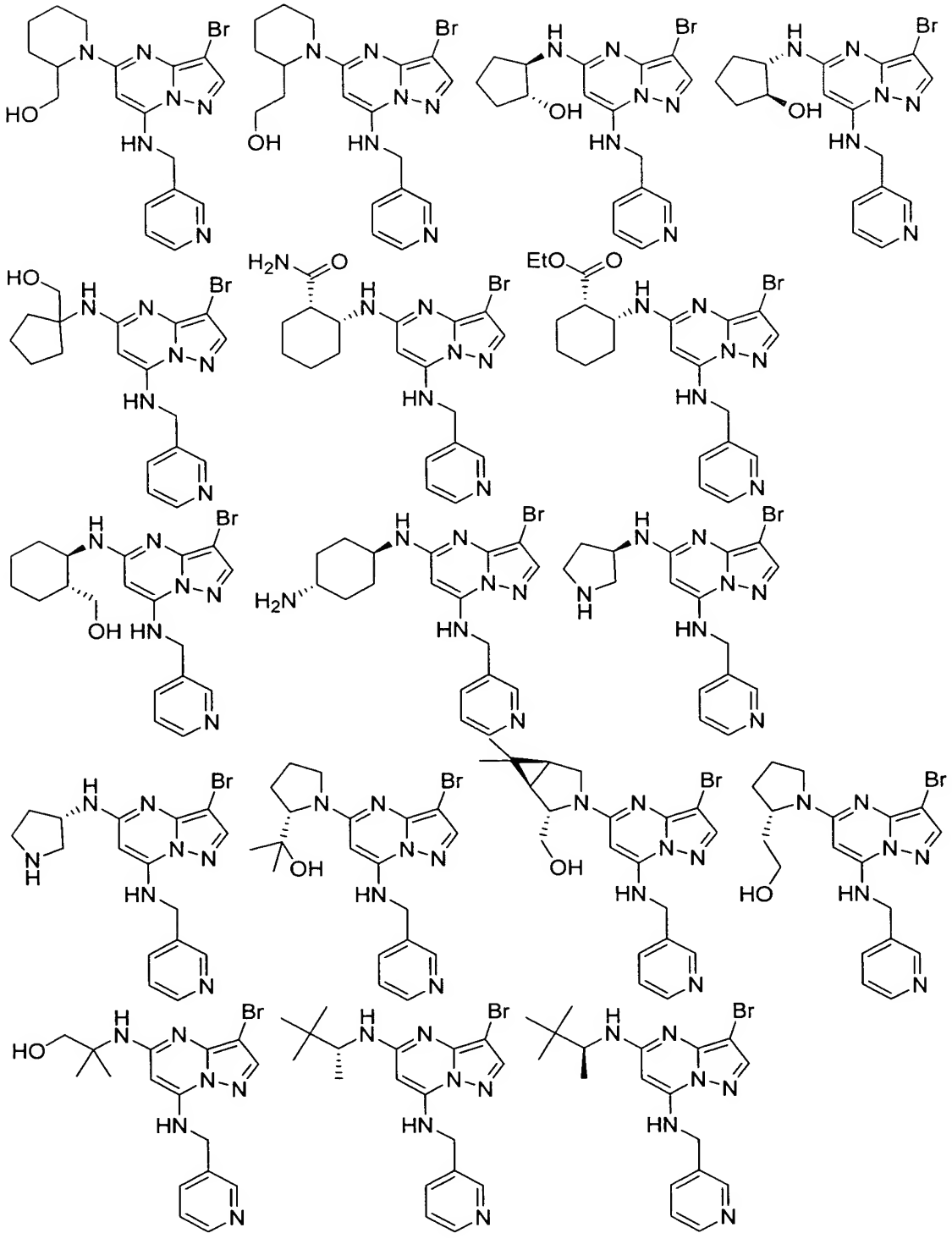


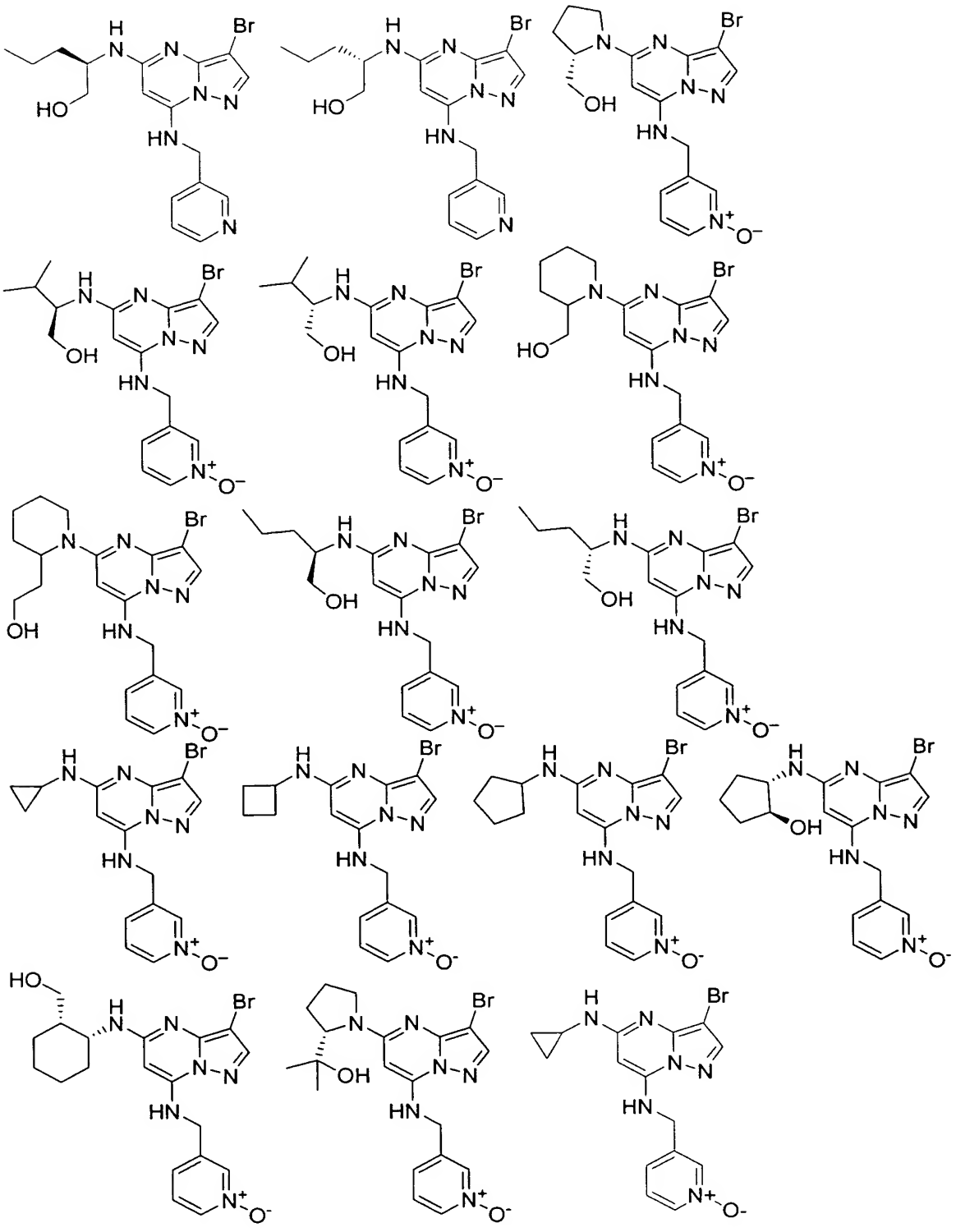


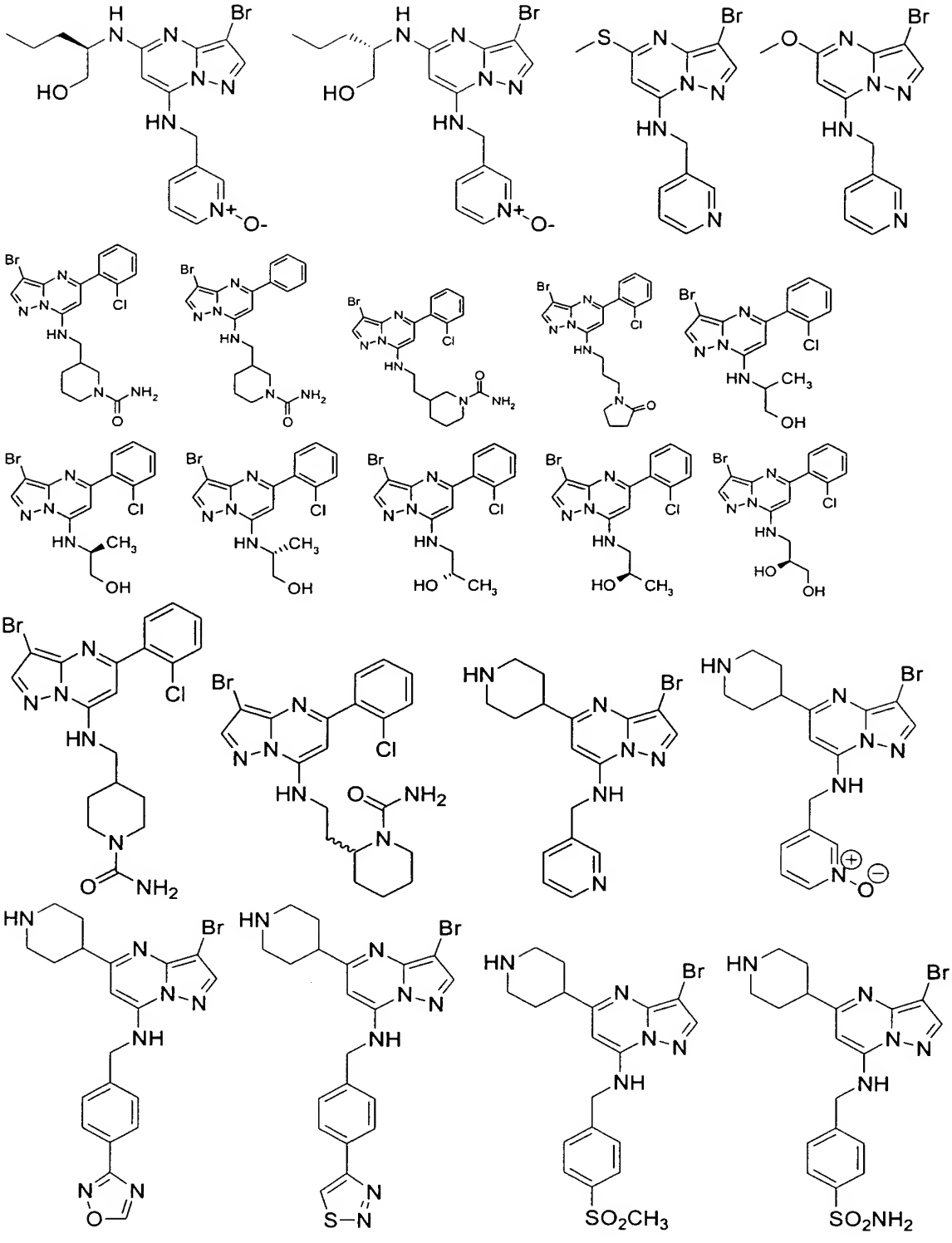


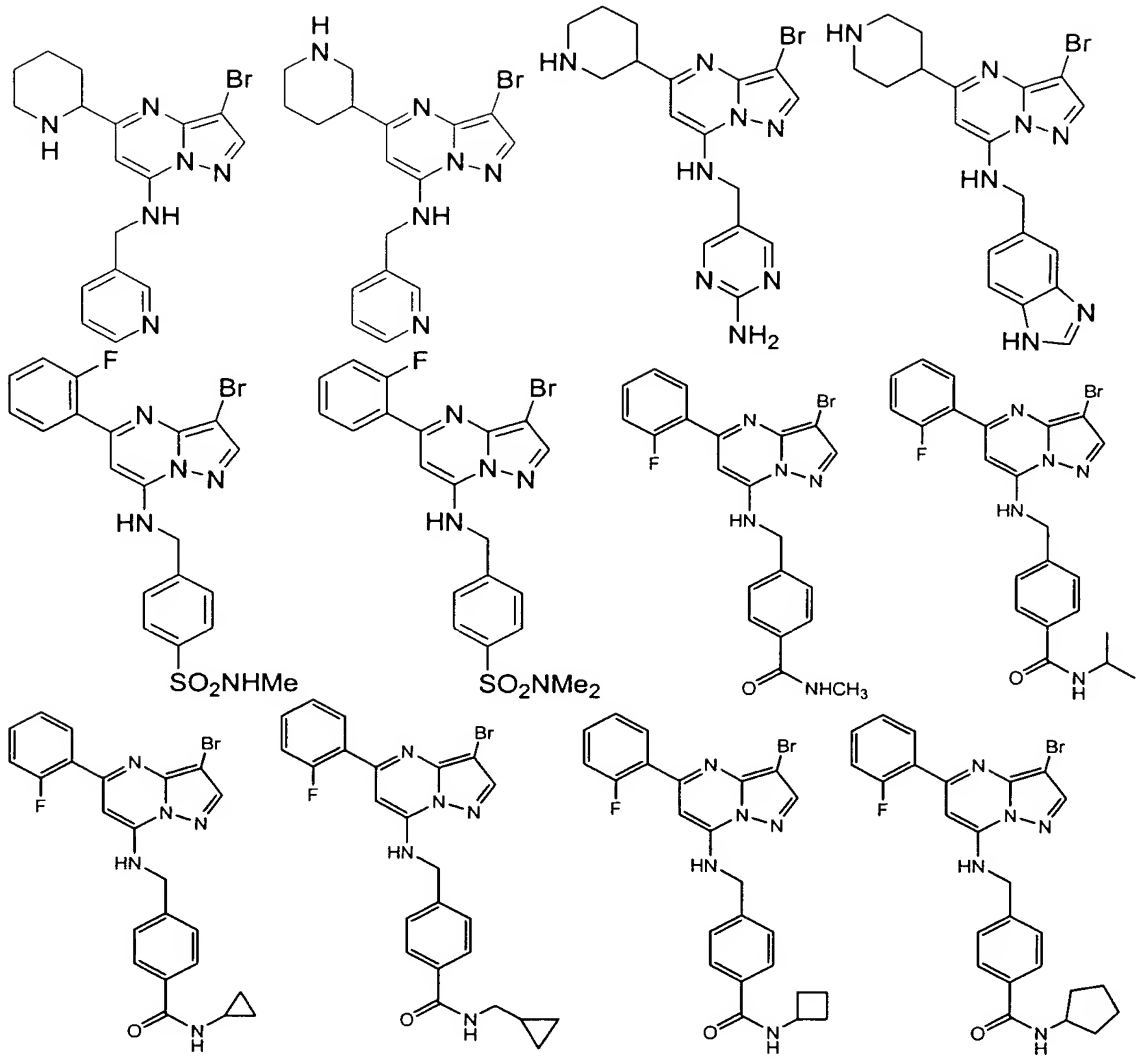


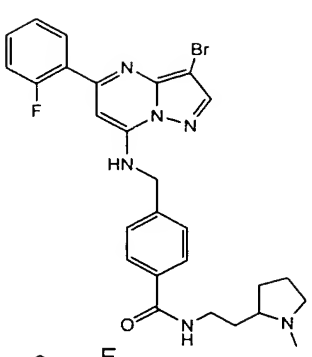


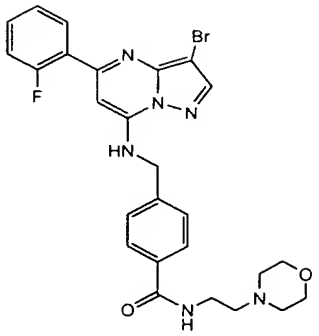


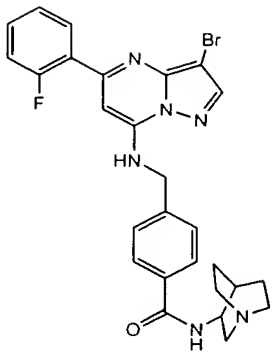


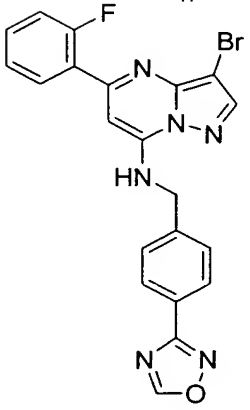


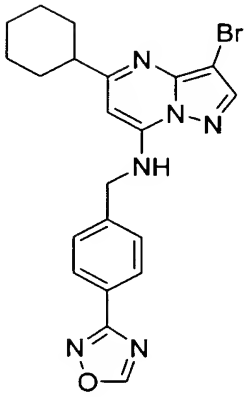

Br
NH
N
H
HN
NH2
F
SO2NHMe
SO2NMe2
NHCH3
O

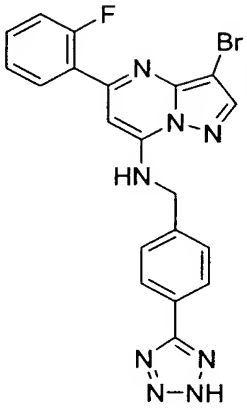


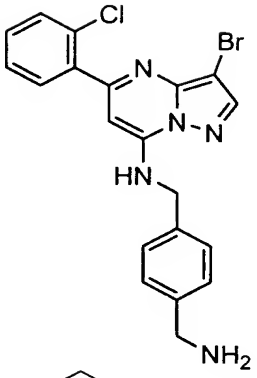


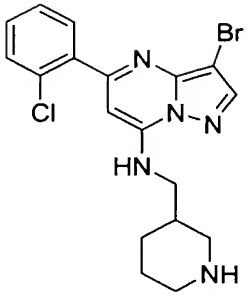


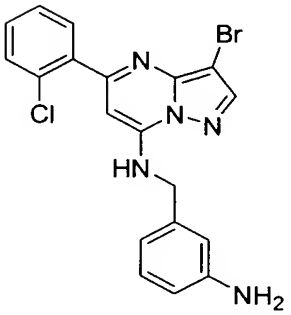


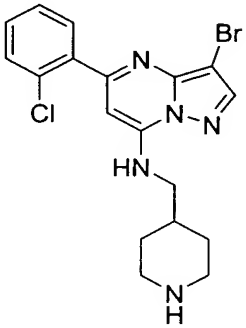


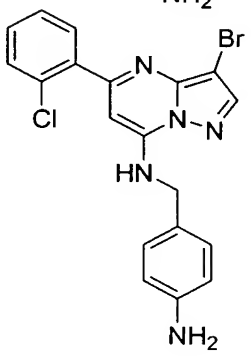


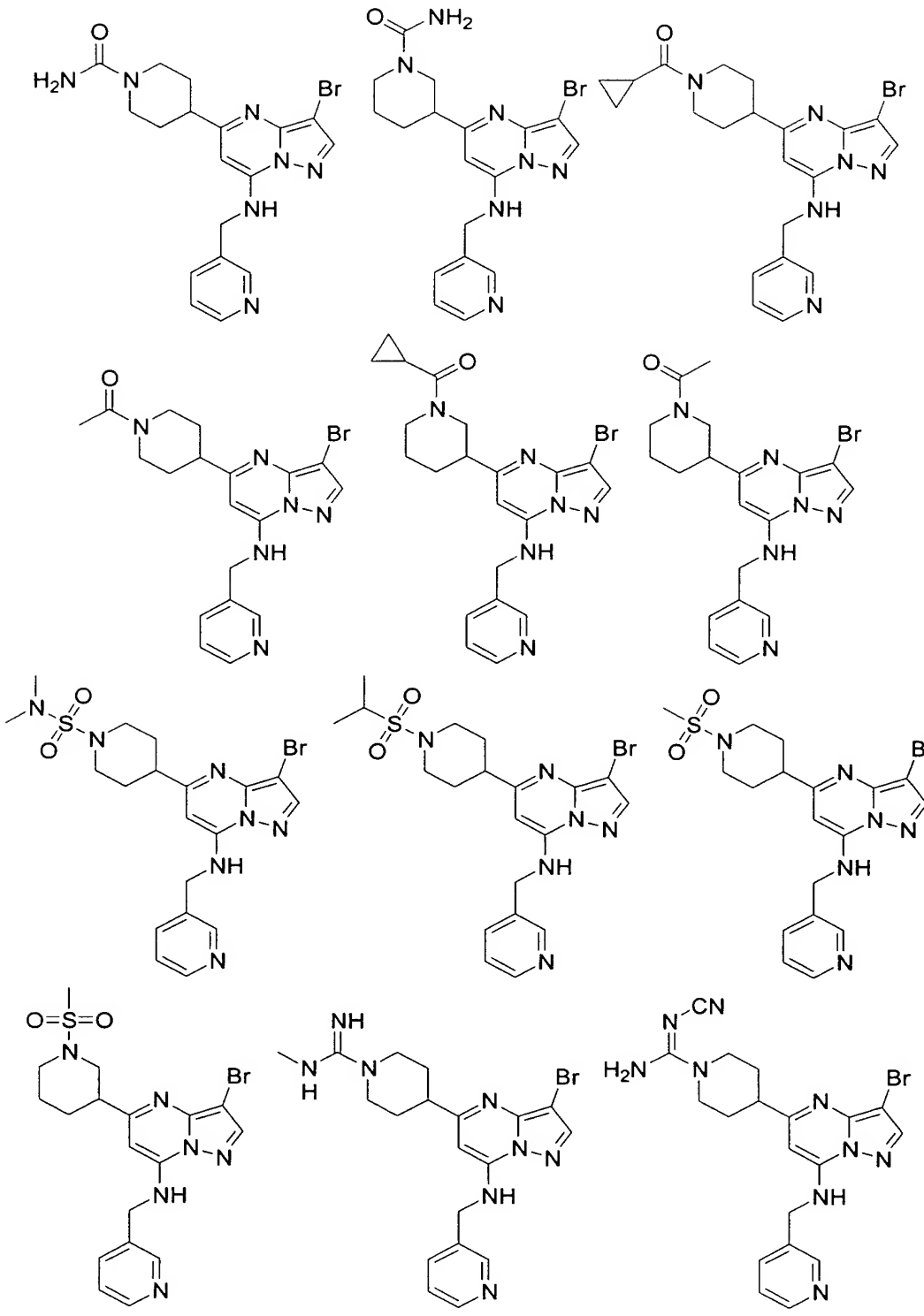


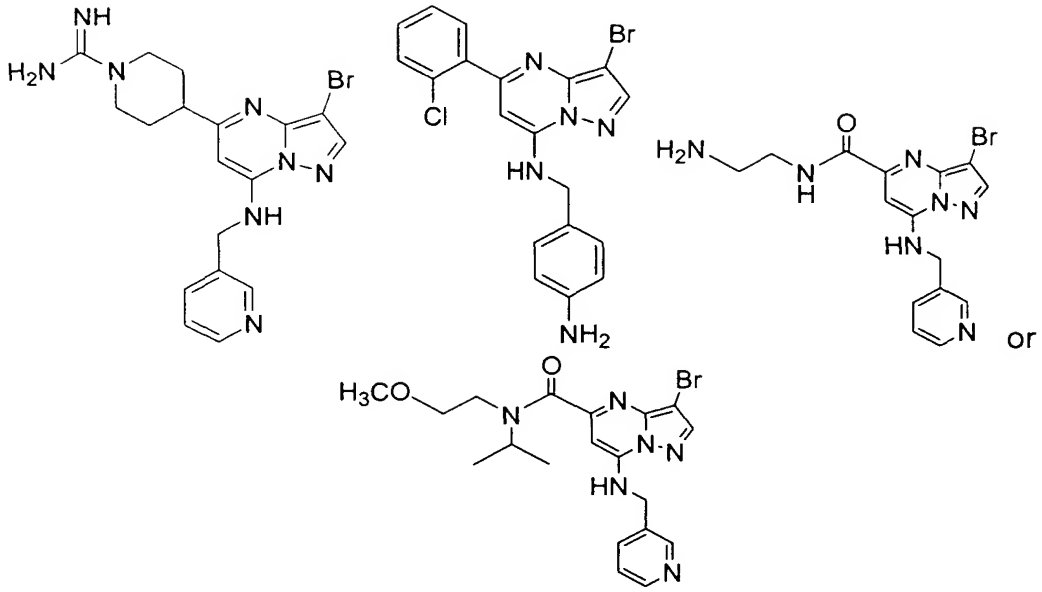






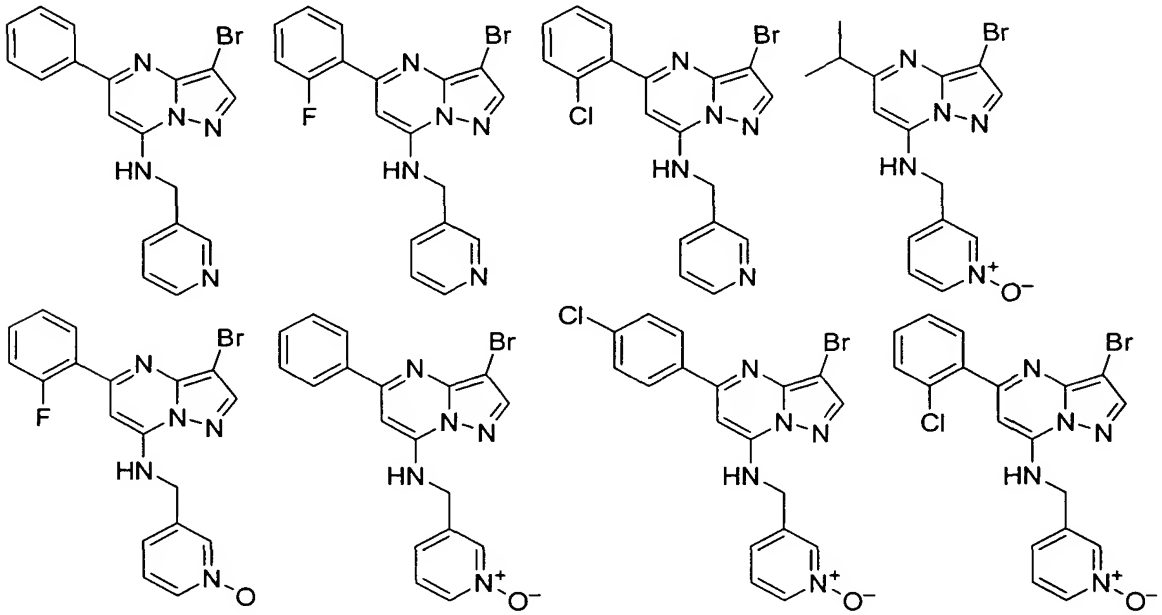


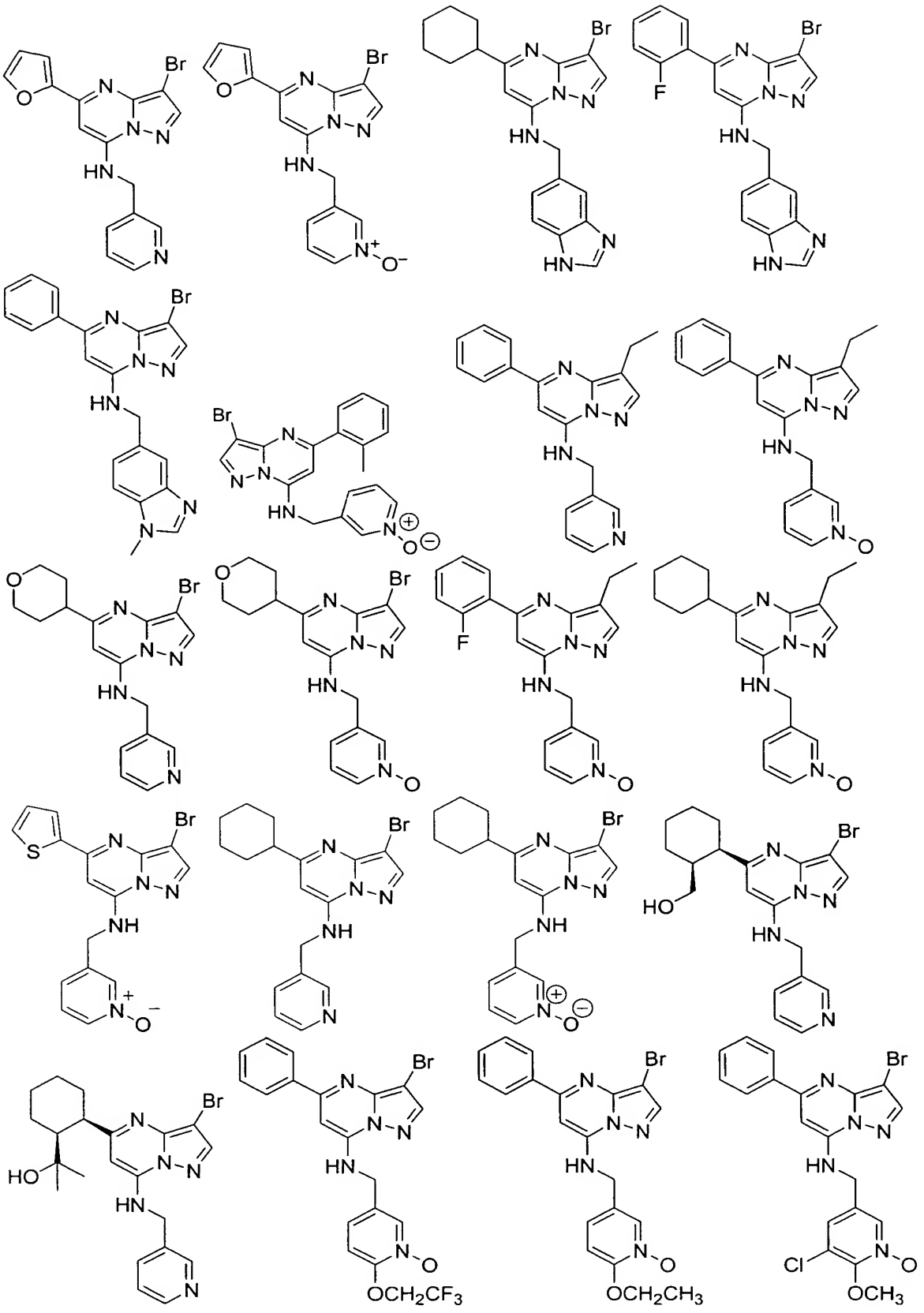


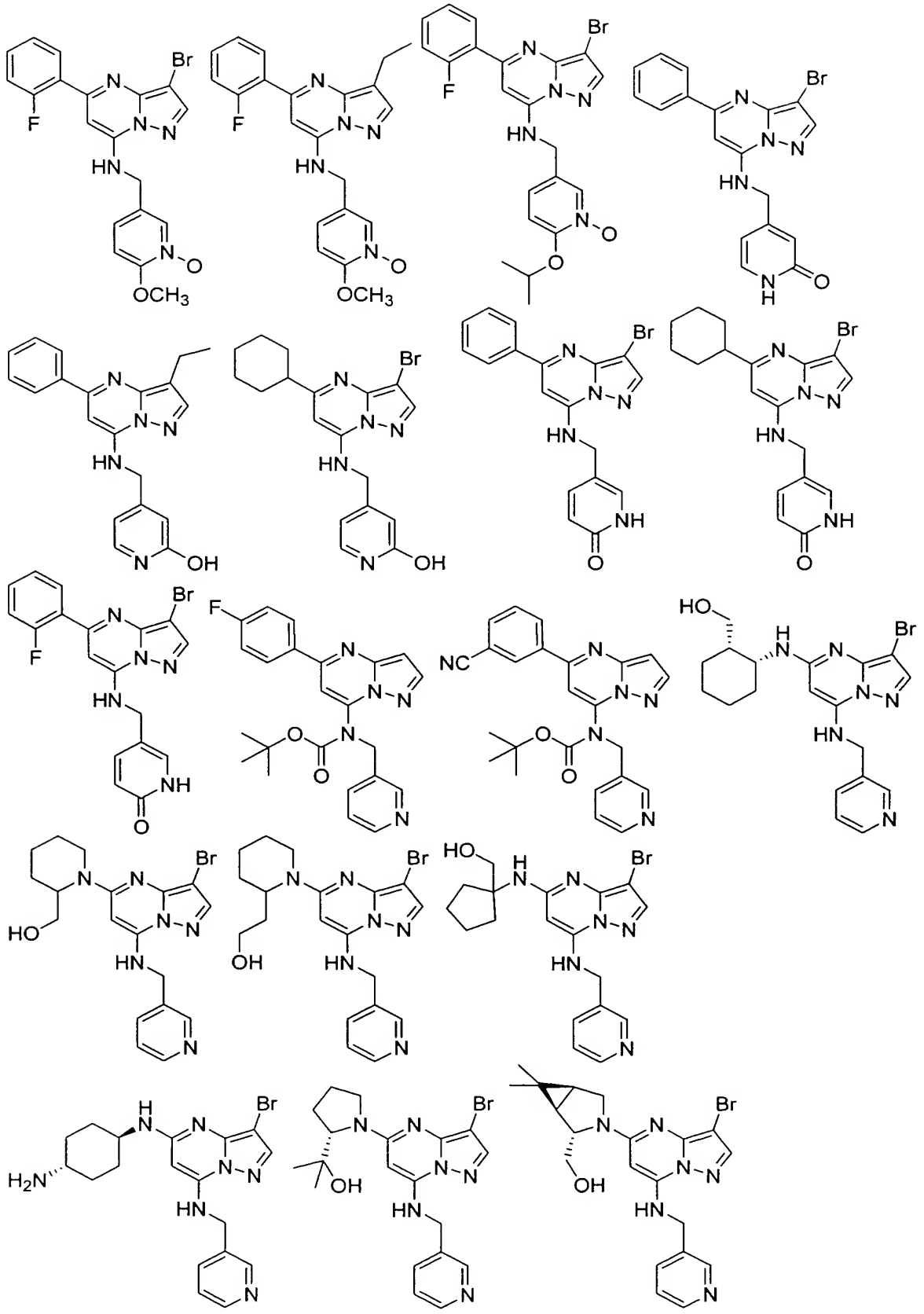


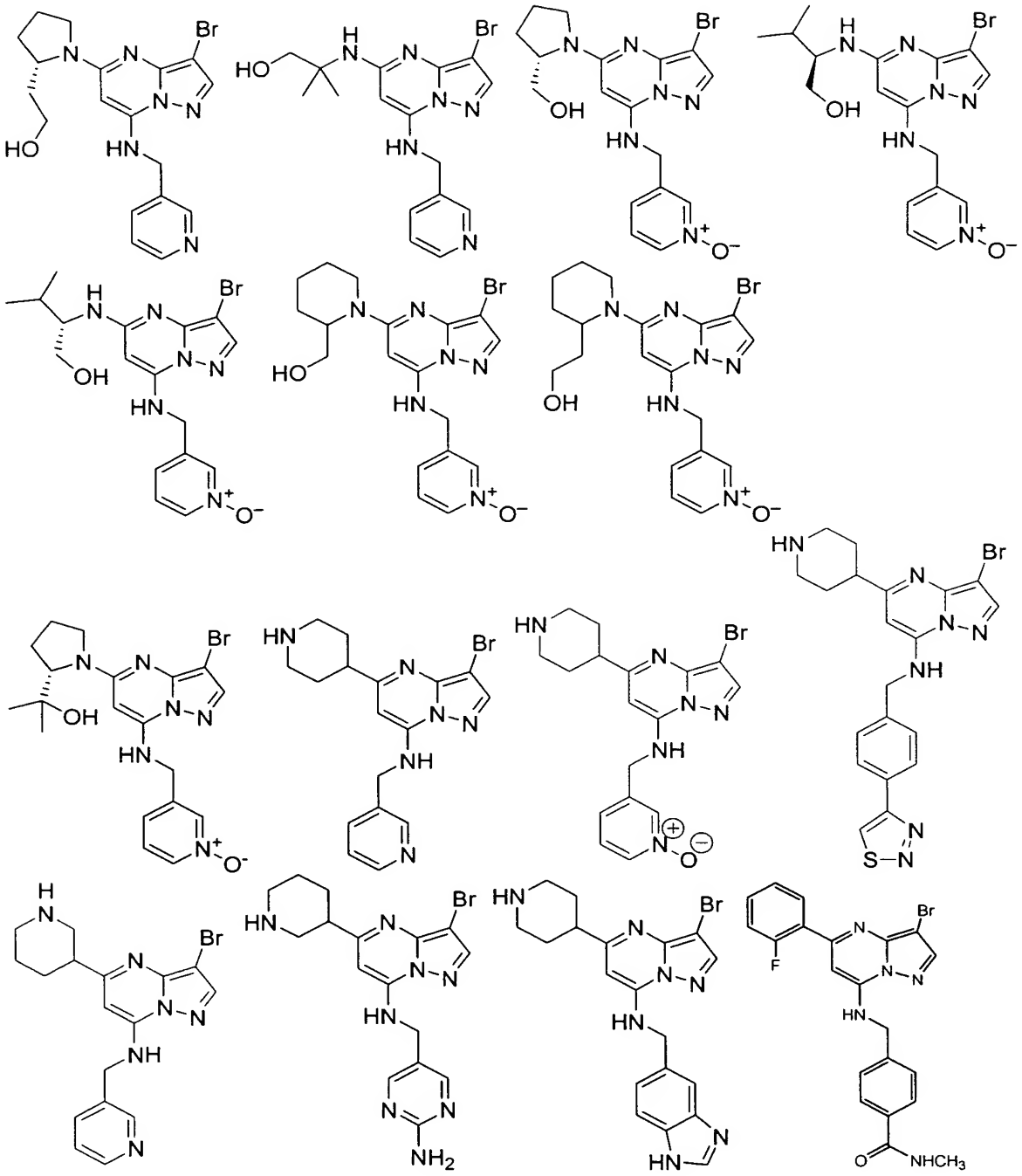
or a pharmaceutically acceptable salt or solvate thereof.

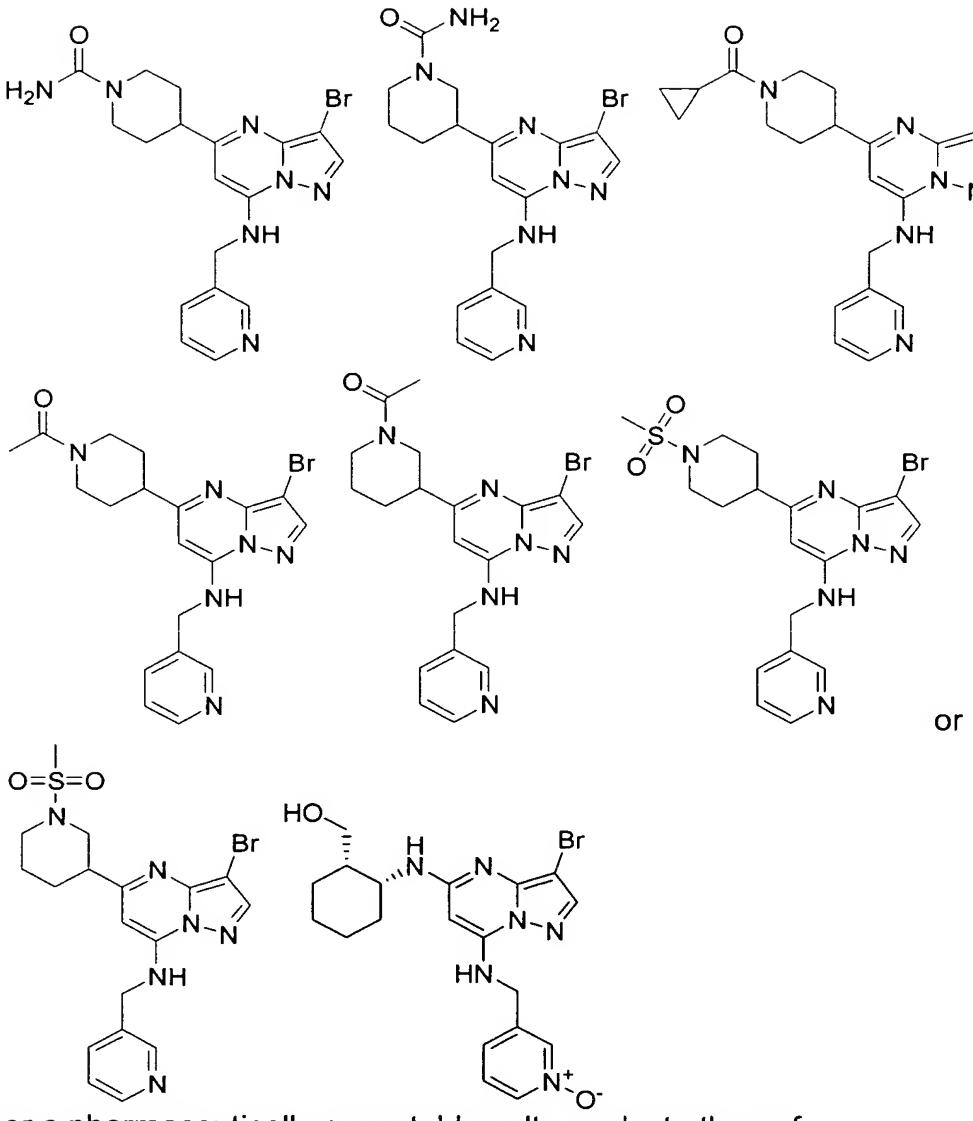
28. A compound of the formula:







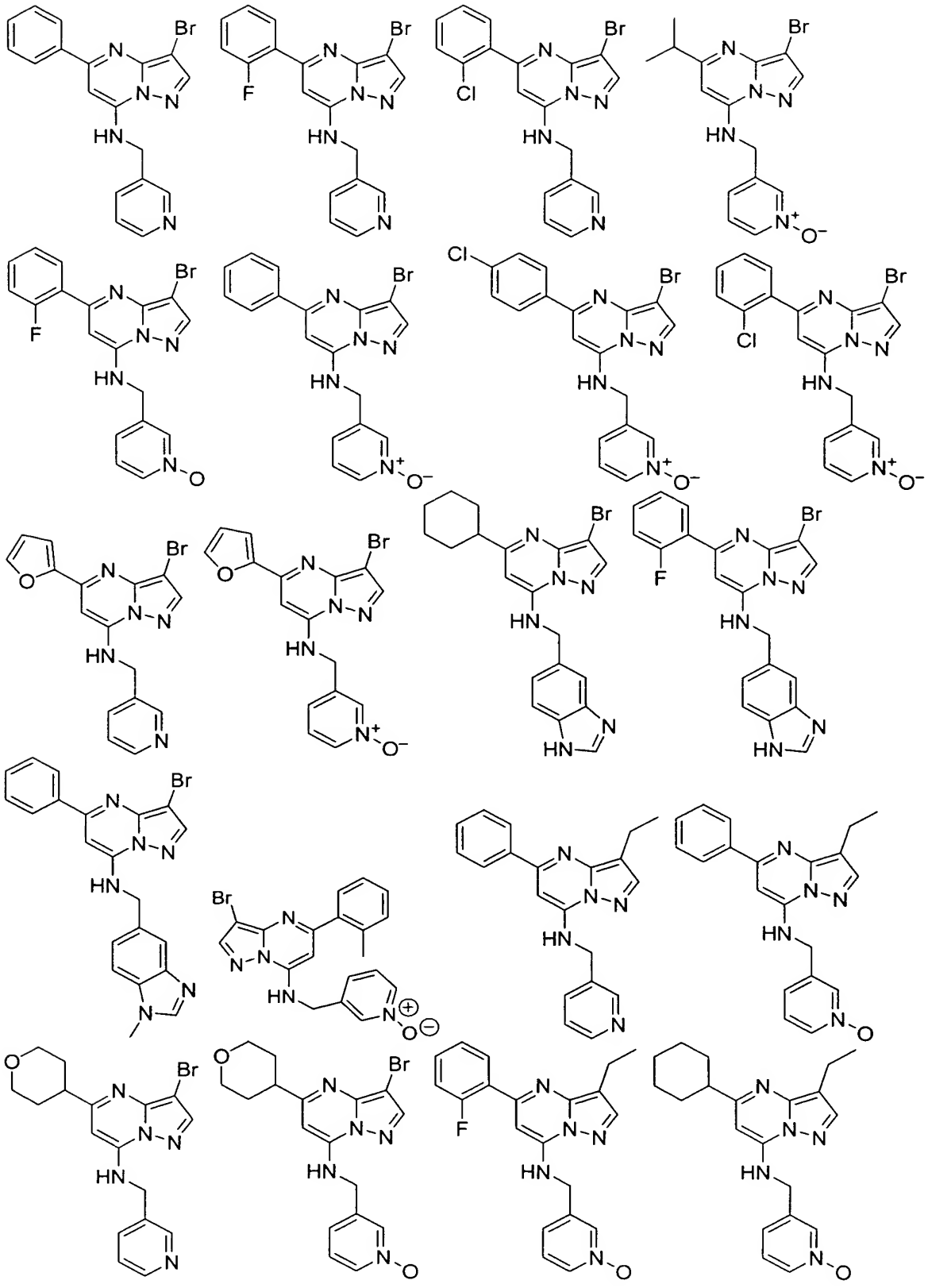


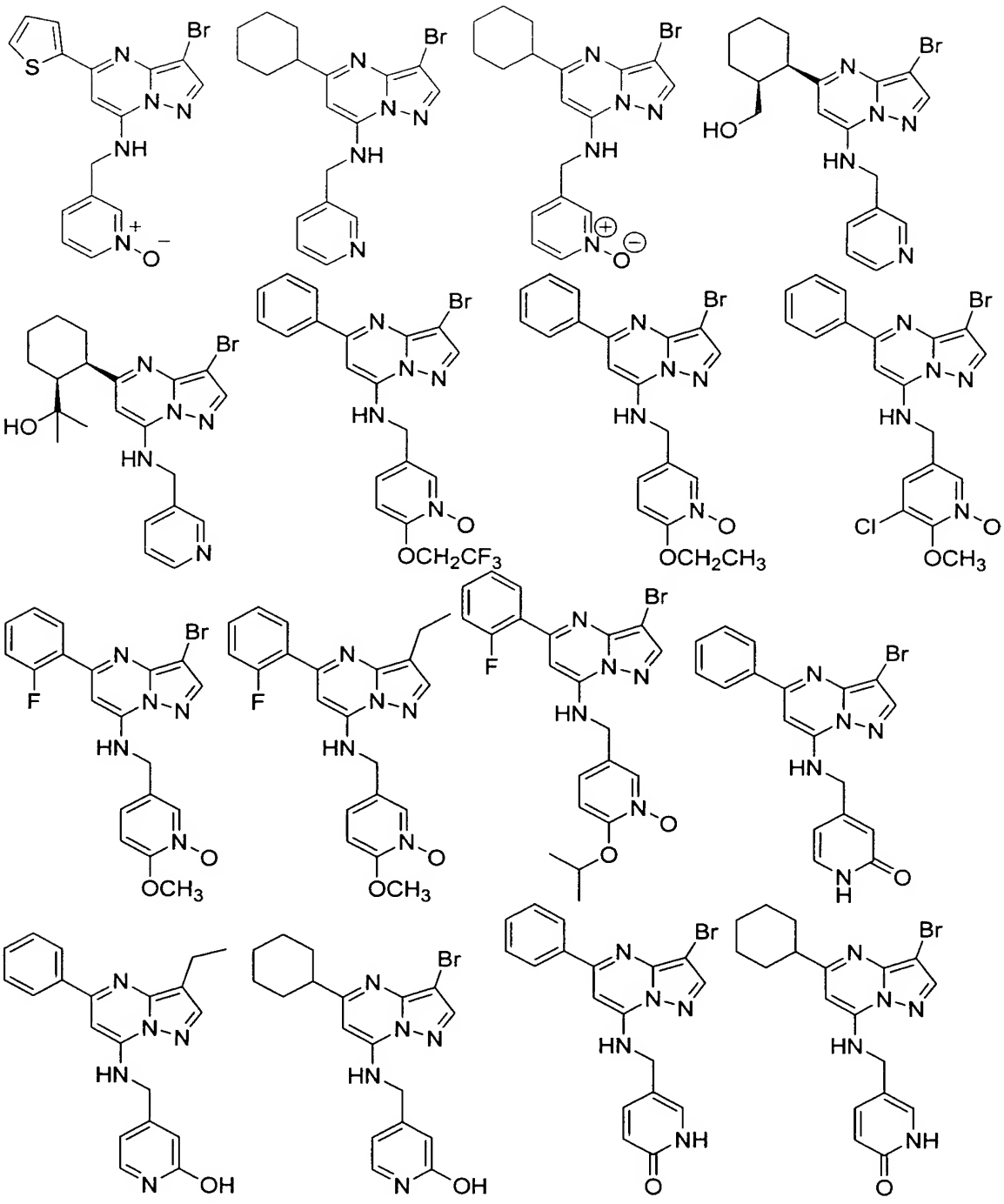


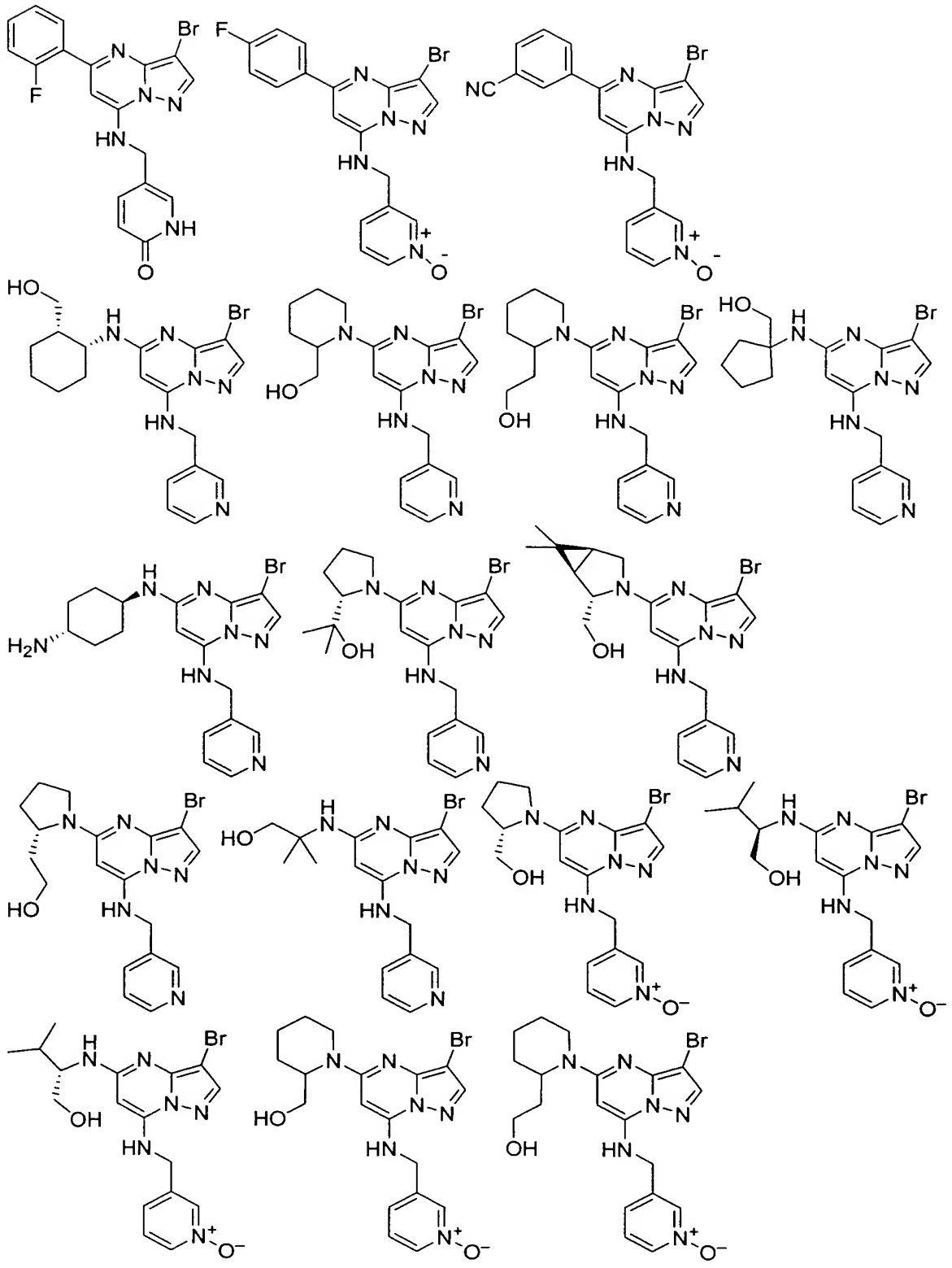
or

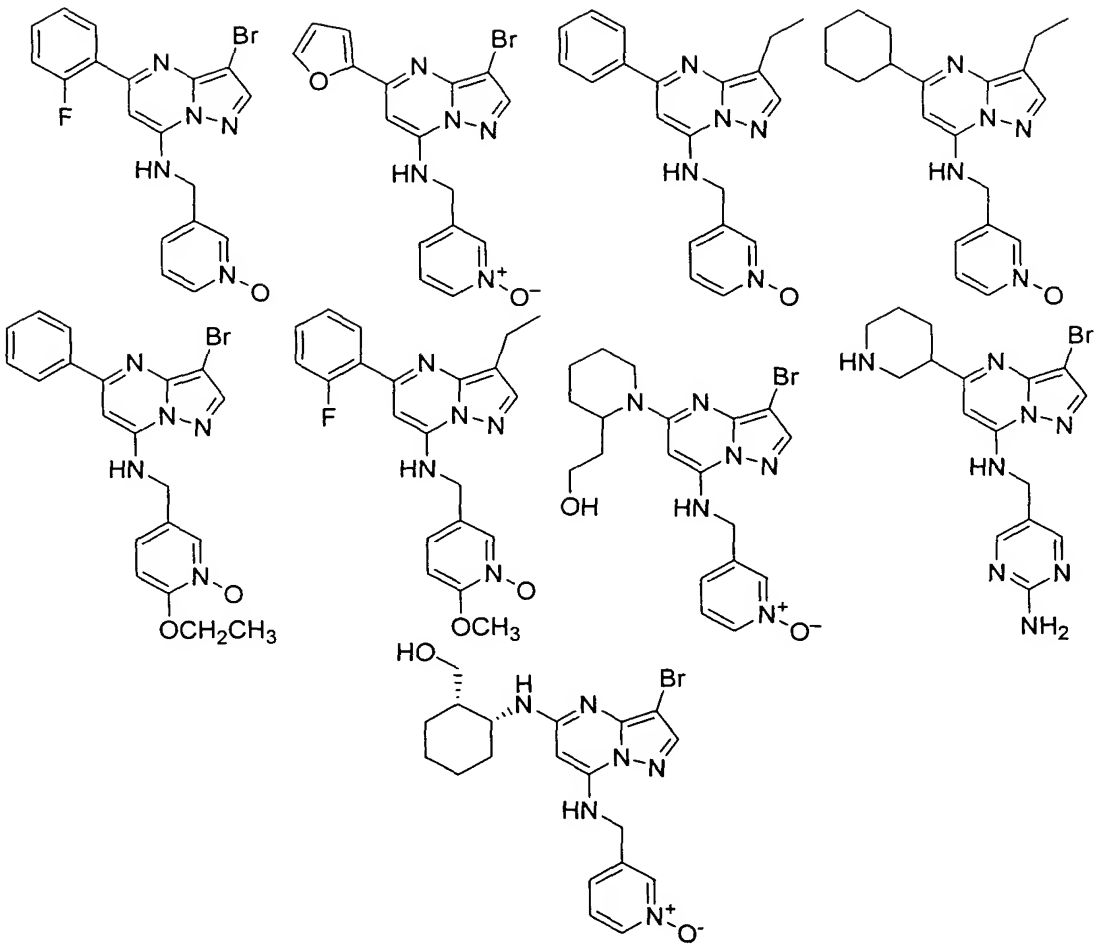
or a pharmaceutically acceptable salt or solvate thereof.

29. A compound of the formula:









or a pharmaceutically acceptable salt or solvate thereof.

31. A method of inhibiting one or more cyclin dependent kinases, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such inhibition.

32. A method of treating one or more diseases associated with cyclin dependent kinase, comprising administering a therapeutically effective amount of at least one compound of claim 1 to a patient in need of such treatment.

33. The method of claim 32, wherein said cyclin dependent kinase is CDK2.

34. The method of claim 32, wherein said cyclin dependent kinase is mitogen activated protein kinase (MAPK/ERK).

35. The method of claim 32, wherein said cyclin dependent kinase is glycogen synthase kinase 3 (GSK3beta).

36. The method of claim 32, wherein said disease is selected from the group consisting of:

cancer of the bladder, breast, colon, kidney, liver, lung, small cell lung cancer, esophagus, gall bladder, ovary, pancreas, stomach, cervix, thyroid, prostate, and skin, including squamous cell carcinoma;

leukemia, acute lymphocytic leukemia, acute lymphoblastic leukemia, B-cell lymphoma, T- cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, hairy cell lymphoma and Burkett's lymphoma;

acute and chronic myelogenous leukemia, myelodysplastic syndrome and promyelocytic leukemia;

fibrosarcoma, rhabdomyosarcoma;

astrocytoma, neuroblastoma, glioma and schwannomas;

melanoma, seminoma, teratocarcinoma, osteosarcoma, xenoderoma pigmentosum, keratoctanthoma, thyroid follicular cancer and Kaposi's sarcoma.

37. A method of treating one or more diseases associated with cyclin dependent kinase, comprising administering to a mammal in need of such treatment

an amount of a first compound, which is a compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof;

and

an amount of at least one second compound, said second compound being an anti-cancer agent;

wherein the amounts of the first compound and said second compound result in a therapeutic effect.

38. The method of claim 37, further comprising radiation therapy.

39. The method of claim 37, wherein said anti-cancer agent is selected from the group consisting of a cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methoxtrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan,

gemcitabine, Uracil mustard, Chlormethine, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, oxaliplatin, leucovirin, ELOXATIN™, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C, L-Asparaginase, Teniposide 17α-Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrazole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine..

40. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of claim 1 in combination with at least one pharmaceutically acceptable carrier.

41. The pharmaceutical composition of claim 38, additionally comprising one or more anti-cancer agents selected from the group consisting of cytostatic agent, cisplatin, doxorubicin, taxotere, taxol, etoposide, CPT-11, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, tamoxifen, 5-fluorouracil, methoxtrexate, 5FU, temozolomide, cyclophosphamide, SCH 66336, R115777, L778,123, BMS 214662, Iressa, Tarceva, antibodies to EGFR, Gleevec, intron, ara-C, adriamycin, cytoxan, gemcitabine, Uracil mustard, Chlormethine, Ifosfamide, Melphalan, Chlorambucil, Pipobroman, Triethylenemelamine, Triethylenethiophosphoramine, Busulfan, Carmustine, Lomustine, Streptozocin, Dacarbazine, Floxuridine, Cytarabine, 6-Mercaptopurine, 6-Thioguanine, Fludarabine phosphate, Pentostatine, Vinblastine, Vincristine, Vindesine, Bleomycin, Dactinomycin, Daunorubicin, Doxorubicin, Epirubicin, Idarubicin, Mithramycin, Deoxycoformycin, Mitomycin-C,

L-Asparaginase, Teniposide 17α-Ethinylestradiol, Diethylstilbestrol, Testosterone, Prednisone, Fluoxymesterone, Dromostanolone propionate, Testolactone, Megestrolacetate, Methylprednisolone, Methyltestosterone, Prednisolone, Triamcinolone, Chlorotrianisene, Hydroxyprogesterone, Aminoglutethimide, Estramustine, Medroxyprogesteroneacetate, Leuprolide, Flutamide, Toremifene, goserelin, Cisplatin, Carboplatin, Hydroxyurea, Amsacrine, Procarbazine, Mitotane, Mitoxantrone, Levamisole, Navelbene, CPT-11, Anastrazole, Letrazole, Capecitabine, Reloxafine, Droloxafine, or Hexamethylmelamine.

42. A compound of claim 1 in purified form.